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Olfactory and gustatory disorders caused by COVID-19: How to regain the pleasure of eating?

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ABSTRACT

Background: Recently, anosmia and ageusia (and their variations) have been reported as frequent symptoms of COVID-19. Olfactory and gustatory stimuli are essential in the perception and pleasure of eating. Disorders in sensory perception may influence appetite and the intake of necessary nutrients when recovering from COVID-19. In this short commentary, taste and smell disorders were reported and correlated for the first time with food science.

Scope and approach: The objective of this short commentary is to report that taste and smell disorders resulted from COVID-19 may impact eating pleasure and nutrition. It also points out important technologies and trends that can be considered and improved in future studies.

Key findings and conclusions: Firmer food textures can stimulate the trigeminal nerve, and more vibrant colors are able to increase the modulation of brain metabolism, stimulating pleasure. Allied to this, encapsulation technology enables the production of new food formulations, producing agonist and antagonist agents to trigger or block specific sensations. Therefore, opportunities and innovations in the food industry are wide and multidisciplinary discussions are needed.

1. Introduction

COVID-19, caused by the SARS-CoV-2 virus, led to a pandemic in March 2020 and a global health crisis (Oliveira, Azeredo, Neri-Numa, & Pastore, 2021; World Health Organization, 2020; Zhou et al., 2020). Due to the high rates of disease transmission, there were more than 100 million deaths worldwide in early 2021, as reported by World Health Organization (WHO) (World Health Organization, 2021). The following symptoms were initially reported: fever, dry cough, headache, nasal congestion, fatigue, breathing difficulties (dyspnea), pneumonia, and, in severe cases, progressive respiratory failure, alveolar damage, and death (Lee et al., 2021; Velavan & Meyer, 2020; Zhou et al., 2020). Only later was the association between COVID-19 and smell and taste disorders during and after the coronavirus infection described (Daher et al., 2020; Giacomelli et al., 2020; Heidari et al., 2020; Lechien et al., 2020; Parma et al., 2020; Russell et al., 2020; Yan, Faraji, Prajapati, Boone, & DeConde, 2020). After reports from countries and regions, such as Brazil, China, Argentina, Chile, South Korea, Iran, Italy, France, Finland, the United Kingdom, and the United States, the WHO considered the loss of smell (anosmia) and taste (ageusia) as a potential marker of the SARS-CoV-2 infection (Lozada-Nur, Chainani-Wu, Fortuna, & Sroussi, 2020; OPAS, 2021; Parma et al., 2020; Zhang, Shan, Abdollahi, & Nace, 2020). Some patients also reported dysgeusia, which is a distortion of the sense of taste (Lozada-Nur, Chainani-Wu, Fortuna, Sroussi, & Oral Surgery Oral Medicine Oral Pathology and Oral Radiology, 2020; Russell et al., 2020). It is noteworthy that another type of coronavirus (SARS-CoV) has presented persistent anosmia as a symptom (Boscolo-Rizzo et al., 2020; Hopkins & Kelly, 2021; Soler, Patel, Turner, & Holbrook, 2020). For SARS-CoV-2, persistent anosmia and ageusia (or variations) even after recovering from COVID-19 has been recently reported (Hopkins & Kelly, 2021; Santos et al., 2021; Soler et al., 2020). There may be a relation between smell and taste disorders with neurological sequelae of the disease, however, further investigations are required (Baig, 2020; Lozada-Nur et al., 2020; Yasuda, 2021).

Olfactory and gustatory stimuli are essential in food perception (Coppin, 2020). Good taste experience while eating relies on smell,

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taste, and chemesthesis (Mastrangelo, Bonato, & Cinque, 2021; Parma et al., 2020). If the sense of smell is lost or compromised, for example, it can lead to microbial risks or food poisoning due to the difficulty in detecting spoiled foods. Besides, it can also cause embarrassment in social environments, which can lead to changes in mood and depression (Coppin, 2020; Croy & Hummel, 2017; Thomas, Baddireddy, & Kohli, 2020). On the other hand, for the recovery of COVID-19 and the well-being of patients, adequate nutrition is required when the senses of smell and taste are preserved (Høier, Chaaban, & Andersen, 2021). Thus, the objective of this short commentary is to present a brief emerging view on the main disorders of smell and taste resulting from COVID-19. Also, it explores, for the first time, how trends and existing technologies in the food industry can help this new consumer regain the pleasure of eating. Databases such as Google Scholar, PubMed, Scielo, ScienceDirect, Scopus, and Web of Science were searched using the following search terms: (i) COVID-19 OR SARS-CoV-2 AND food AND anosmia OR dysosmia OR ageusia OR dysgeusia; (ii) COVID-19 OR food OR sensory food AND texture OR natural dye OR encapsulation; (iii) dysgeusia AND undesirable odors OR undesirable flavors OR encapsulation, in the title, abstract and keywords. As a result, 75 studies published in 2020–2021 were included.

2. COVID-19: olfactory and taste disorders

Anosmia is the complete loss of smell, while hyposmia is the partial or reduced ability to smell and detect odors (Desai & Oppenheimer, 2021). Anosmia is commonly associated with viral infections of the upper respiratory tract, *e.g.*, common cold, influenza: (i) influenza virus, (ii) parainfluenza, and (iii) rhinovirus (Soler et al., 2020). Anosmia caused by SARS-CoV-2 has also been reported (Hwang, 2006). A previous epidemiological study showed that 85.6% of 417 patients with COVID-19 had olfactory dysfunctions (Lechien et al., 2020). Yan et al. (2020) analyzed a larger group of 858 patients with COVID-19 and reported that 68% had anosmia as a symptom. In healthy people, olfactory chemosensation is mediated by the olfactory nerve (CN I) and the trigeminal nerve (CN V) (Thomas et al., 2020). Briefly, the detection of smell occurs when the olfactory receptor cells in the upper nasal cavity bind to the odoriferous molecules, and then a signal is transported through primary afferent neurons until it reaches the olfactory bulb (Novaleski et al., 2021; Thomas et al., 2020). In turn, in the olfactory bulb, there is a synapse with second-order neurons responsible for taking the received stimuli to the upper olfactory centers of the brain (cerebral cortex), where smell is detected (Desai & Oppenheimer, 2021; Negoias et al., 2010; Thomas et al., 2020). Regarding the contamination by SARS-CoV-2, there is an exacerbation of the inflammatory response in the nasal cavity, which temporarily prevents smell from reaching the olfactory receptor neurons (Soler et al., 2020). Research shows that the SARS-CoV-2 RNA has been found mainly in the olfactory mucosa, besides other olfactory regions such as the olfactory bulb, uvula, trigeminal ganglion, and medulla (Lemprière, 2021; Meinhardt et al., 2021). The recovery from anosmia can vary and depends on the area affected, resulting in persistent symptoms. For example, the epithelial tissue recovers faster than olfactory neurons. In this case, axon regeneration would be required to make effective synapses with the olfactory bulb, which may take months or years (Soler et al., 2020).

Dysosmia has also been reported as an olfactory disorder in COVID-19 patients (i) as a distortion of olfactory perception (*e.g.*, parosmia and cacosmia) or (ii) as the detection of smells that are not present in the environment (*e.g.*, phantosmia or olfactory hallucinations) (Doty & Bromley, 2007; Parma et al., 2020). Dysosmia can be caused by incomplete regeneration in olfactory neurons or the malfunction of primary olfactory centers in the brain, especially the olfactory bulb (Yousefi-Koma, Haseli, Bakhshayeshkaram, Raad, & Karimi-Galougahi, 2021). Recently, a study showed that 35.9% of the 217 patients diagnosed with COVID-19 had dysosmia, with recovery ranging between 2 and 35 days (Sheng, Liu, Wang, Chang, & Chang, 2021). Sheng et al. (2021) also reported that 10.2% of patients had persistent dysosmia. Another prospective multicenter cohort study with 145 COVID-19 patients described that dysosmia persisted for at least 95 days (Li et al., 2020).

Regarding taste disorders, ageusia is characterized by a complete loss of taste function, which may be due to: (i) transport problems of tastants to the taste buds (*e.g.*, chronic oral dryness) or damage to pores of taste (*e.g.*, from inflammation or burns) (Desai & Oppenheimer, 2021; Doty, 2014). Recently, ageusia was considered one of the main COVID-19 symptoms (Desai & Oppenheimer, 2021; Giacomelli et al., 2020; Lechien, Cabaraux, et al., 2020; Yan et al., 2020). A previous study showed that 24.1% of 141 young patients (average age of 15.2 years) lost their taste when infected with COVID-19 (Kumar et al., 2021). Higher percentages of ageusia (71%–88.8%) were reported in older patients (mean 39.17–48.5 years) infected with SARS-CoV-2 (Lechien et al., 2020; Yan et al., 2020). It is known that healthy taste is perceived through the activation of specialized taste cells, mainly in the lingual papillae. The sensation is transmitted via the facial nerve (NC VII), the glossopharyngeal nerve (NC IX), and vagus nerve (NC X), allowing primary sensory qualities of flavor (sweet, salty, bitter, sour, kokumi, and *umami*) (Mastrangelo et al., 2021; Novaleski et al., 2021). The receptor for SARS-CoV-2 is the angiotensin-converting enzyme 2 (ACE2), found in the epithelium of the taste buds and the salivary glands (H. Xu et al., 2020). Therefore, human salivary glands are affected early by the SARS-CoV-2 infection, resulting in their dysfunction and subsequent impairment of the salivary flow (Lozada-Nur et al., 2020). The gustatory system can be affected by the viral lytic pathway in two ways, namely: (i) with direct damage to the ACE2 cells in the taste buds and peripheral neurosensory chemoreceptors, or (ii) with direct damage to any of the nerves skulls responsible for the taste (CN VII, IX or X), resulting in damage to the taste perception during COVID-19 (Finsterer & Stollberger, 2020).

Dysgeusia (synonym: parageusia) is another taste disorder, often unpleasant, which causes distortion in the quality of taste and has also been related to COVID-19 (Desai & Oppenheimer, 2021; Frank & Barry, 2016; Lozada-Nur et al., 2020). As already mentioned, SARS-CoV-2 binds to ACE2 receptors on the oral mucosa, triggering an inflammatory response (Lozada-Nur et al., 2020; Xu et al., 2020). In turn, the inflammatory response of taste cells is expressed by signaling inflammatory cytokines, such as interferon (IFN) (Hong Wang, Zhou, Brand, & Huang, 2009). IFN can trigger apoptosis and cause abnormal renewal in the taste buds, leading to the development of taste dysfunction (Lozada-Nur et al., 2020). In addition, the immaturity of newly formed neural networks can also lead to parageusia (Mastrangelo et al., 2021). Studies correlating dysgeusia and COVID-19 are still scarce; however, it has been recently reported that 62% of 217 patients infected with SARS-CoV-2 showed dysgeusia symptoms, with an average recovery of 12 days (Sheng et al., 2021). There are reports of delayed dysgeusia after COVID-9 due to the association of these disorders with neurological sequelae, yet further investigations are required (Lozada-Nur et al., 2020; Santos et al., 2021; Soler et al., 2020; Yasuda, 2021).

3. Relating COVID-19 with food sensation

Anosmia or ageusia (and their variations) resulting from COVID-19 brought a global awareness of the loss of sensory senses, including those directly linked to food-evoked emotions (Coppin, 2020). It is known that smell and taste detect chemical stimuli and convert them into electrical energy to be perceived by the central nervous system. They also contribute to a complete sensation of taste (Thomas et al., 2020). Through olfactory sensory neurons in the nasal cavity, the olfactory system detects volatile chemical compounds in two ways: (i) odor, to detect smell from the external environment; (ii) retronasal smell, to perceive flavor dimensions of food or drinks (Croy et al., 2014; Kang, Cho, Lee, Kim, & Park, 2020). The gustatory system, in turn, perceives the tastes of sweet, salty, bitter, sour, and *umami* from non-volatile compounds, and the chemesthesis detects sensations such as burning, cooling, or tingling, *e.g.*, in herbs or spices (Kang et al., 2020; Parma et al., 2020). Notably, in individuals with loss of the retronasal smell, the hedonic value of food is drastically reduced (Coppin, 2020). As reported by Coppin (2020), when eating a strawberry, for example, an individual with anosmia may perceive sweet/sour taste (due to the gustatory input), but the complete and synesthetic natural flavor of strawberry will not be perceived, due to the lack of retronasal olfactory input. Taste tests have shown the worst overall rates for sweet and bitter taste perception in patients with COVID-19 (Desai & Oppenheimer, 2021; Soler et al., 2020).

Taste perception is also closely associated with the metabolic action of peptidases, such as ACE2 and APN (amino and carboxypeptidases, respectively) (Ardö, 2006; Luchiari, Giordano, Sidman, Pasqualini, & Arap, 2020; Hongliang Wang et al., 2008). ACE2 and APN promote proteolytic cleavage of proteins, leading to the formation of different amino acids. Each has specific flavors (*e.g.*, glutamate has umami flavor and L-amino acids that trigger bitter taste) (Choudhuri, Delay, & Delay, 2015). According to Luchiari et al. (2020), since SARS-CoV-2 binds to ACE2, the virus enters the cell, causing: (i) reduced availability of ACE2 in the cell membrane, (ii) inactivation of taste receptors. In other words, the internalization of the receptor (ACE2) by the coronavirus infection in the taste buds leads to the loss of taste (Luchiari et al., 2020). Likewise, APN is also expressed in the tongue and is associated with taste transduction (Yoshida et al., 2018). As SARS-CoV-2 infects nasal and oral epithelia, other molecules involved in flavor processing and signal transduction can be impaired in infected cells, leading to ageusia in COVID-19 patients (Luchiari et al., 2020).

Loss of taste and/or smell can affect the quality of life, nutrition, and safety (Desai & Oppenheimer, 2021). The importance of sensory properties for the hedonic perception of food is evident and proven by a wide range of studies and models (Aguayo-Mendoza, Chatonidi, Piqueras-Fiszman, & Stieger, 2021; Jürkenbeck & Spiller, 2021; Yang et al., 2021). For example, memories and emotions are closely linked to smell. They also play an important role in the wellbeing, reducing stress and depression (Coppin, 2020; Oleszkiewicz, Kunkel, Larsson, & Hummel, 2020; Olofsson, Ekström, Larsson, & Nordin, 2021; Rabin, 2021; Willander & Larsson, 2007). Sensory dysfunction can cause a decrease in appetite and the intake of essential nutrients for a rapid recovery of COVID-19, leading to weight loss, malnutrition, and excessive intake of salt or sugar (Høier et al., 2021; Soler et al., 2020; Thomas et al., 2020). In addition, smell disorders decrease the ability to detect food safety hazards, such as spoiled food, especially stored food (Desai & Oppenheimer, 2021; Moini & Piran, 2020).

Some solutions to improve the quality of life in patients with anosmia and parosmia after COVID-19 have been proposed, such as olfactory training, which involves actively sniffing the same scents in order to train the brain and induce the ability to identify odors (Walsh-Messinger, 2021). For example, the meta-analysis by Sorokowska, Drechsler, Karwowski, and Hummel (2017) suggested that smell training was useful for improving general olfactory function. The method is also promising for the recovery of parosmia (Liu et al., 2021). However, there are still few discussions and trends specifically proposed by the food sectors aimed at patients with smell and taste disorders.

4. Recreating sensory texture for patients with anosmia and ageusia

Understanding the association between food rheological behaviors and sensory experience is one of the main challenges in food research (Bolhuis & Forde, 2020; Joyner, 2018). Food texture (which includes viscosity, hardness, elasticity, among others) is a set of mechanical, geometric, and superficial attributes that can be perceived through mechanical, tactile, and, when appropriate, visual, and auditory modalities. They are also perceived during the conversion of the food structure into *bolus* through a complex series, which involves ingestion, processing, lubrication, and swallowing (Joyner, 2018; van Eck & Stieger, 2020). Unlike aroma and taste, which are associated with specific molecular structures, food texture is a cognitive property based on the interaction of different senses (touch, hearing, and vision) (Pascua, Koç, & Foegeding, 2013; van Eck & Stieger, 2020).

It has been previously reported that harder foods, for example, can help prolong chewing and taste, which can be positive for patients with anosmia and ageusia (de Graaf, 2020; Joyner, 2018; Laguna, Fiszman, & Tarrega, 2021). In addition, these foods increase chewing, reduce overeating rates and promote satiety (Bolhuis & Forde, 2020; Ohkuma et al., 2015; Robinson et al., 2014). Investing in firm, crunchy food textures that stimulate the trigeminal nerve during ingestion can increase appetite and pleasure (Frasnelli & Hummel, 2007; Høier et al., 2021). However, it is noteworthy that texture preferences can be different due to regional variation of taste. In general, crunchy solid foods (*e.g.*, grains, cereals, hard vegetables, and crispy snacks) are good options for individuals with anosmia and ageusia since prolonged taste and crunching can stimulate and make eating more satisfying (Morrison, 2021; Zhang, 2021). Another option is to consume foods with different textures in order to improve tactile interaction and pleasure, instead of consuming more foods or adding sugar, salt, or fat to the diet (Burges Watson et al., 2020; van Eck & Stieger, 2020). Different textures lead to continuous transitions of food structures, resulting in intraoral sensory variety during intake and consumer appreciation (van Eck & Stieger, 2020). The addition of hydrocolloids, such as proteins and polysaccharides, can help obtain textures that result in enhanced palatability (Seisun & Zalesny, 2021). Grains and dry foods can be added to the food matrix for a wide diversity of textures (Barrett, Foster, & Beck, 2020). Therefore, consuming different textures can lead to a more satisfying and nutritious eating experience (Morrison, 2021).

In this scenario, the food industry must adapt and create opportunities, investing in different food textures combined with strong flavors (*e.g.*, pepper, wasabi, ginger, and others) (Morrison, 2021; Zhang, 2021). Particularly, spices (*e.g.*, cinnamon, vanilla, chili, jambu - *Acmella oleracea*, wasabi, and others) can also add complexity to the eating experience (Bolhuis & Forde, 2020; Morrison, 2021).

5. Challenges and future trends

Some existing trends and technologies in the food industry can improve the food experience, such as the use of natural dyes. The sense of sight mediated by attention, pleasure, and reward systems, plays an important role in eating (Spence, Okajima, Cheok, Petit, & Michel, 2016). In this sense, the use of dyes (mainly natural) can increase acceptability and add functional properties to foods (Isabel, Neves, Silva, & Meireles, 2021). Natural dyes can contribute to enhancing the colors of foods, such as (i) iridoid blue (from *Genipa americana* L.) (Neri-Numa, Angolini, Bicas, Ruiz, & Pastore, 2018) (ii) bixin (Bachtler & Bart, 2021; Beni et al., 2020; Xu & Kong, 2017), (iii) anthocyanins (Becerril, Nerín, & Silva, 2021; Coelho Leandro et al., 2021), (iv) betalains (Lima et al., 2020; Shunan, Yu, Guan, & Zhou, 2021; Sravan Kumar, Singh Chauhan, & Giridhar, 2020), (v) chlorophylls (Ribeiro & Veloso, 2021), (vi) caramel (Beata Olas, Urbańska, & Bryś, 2020), (vii) curcumin (Song & McClements, 2021; Tian Jiang, Raja Ghosh, 2021), (viii) carminic acid (Neves et al., 2021), (ix) lycopene (Allison & Simmons, 2017; Pataro, Carullo, Falcone, & Ferrari, 2020) e (x) carotenoids (Rodriguez-Amaya, 2019), among others. A previous study reported that colorful foods increased the modulation of brain metabolism by 24% and stimulated eating (Spence et al., 2016). Vibrant colors can have a direct positive effect on mood in people with olfactory and gustatory disorders (Moini & Piran, 2020). A diet rich in colorful foods improves nutrition which is important for the recovery from COVID-19 (Jalil, Yunus, & Said, 2012).

As previously reported, dysosmia and dysgeusia are unpleasant disorders that cause distortion or error in the original quality of aroma and taste, respectively. In this context, the encapsulation of flavor and aroma of foods can be an important technology since it successfully masks flavor and aroma compounds (de Oliveira et al., 2021; Oliveira et al., 2020; Saifullah, Shishir, Ferdowsi, Tanver Rahman, & Van Vuong, 2019). Some foods or their volatile compounds have already been encapsulated to mask undesirable flavors and odors: (i) pea protein (Cui, Kimmel, Zhou, Rao, & Chen, 2020); (ii) oils in general (fish, shrimp, cod liver, garlic, green coffee, etc.) (Gulzar & Benjakul, 2020; Morsy & Elsabagh, 2021; Oliveira et al., 2020; Pourashouri, Shabanpour, Heydari, & Raeisi, 2021; Raeisi, Ojagh, Pourashouri, Salaün, & Quek, 2021; Serfert, Drusch, & Schwarz, 2010); (iii) astaxanthin (Martínez-Álvarez, Calvo, & Gómez-Estaca, 2020); (iv) catechin (Astray, Mejuto, & Simal-Gandara, 2020); (v) bitter acids (caffeine, quinine, and chlorogenic) (Astray et al., 2020); (vi) bioactive peptide powder (Wang & Selomulya, 2020), among others. Currently, there are no products developed by the industry or described in the literature concerning flavor and aroma encapsulation for consumers with dysosmia and dysgeusia. Given that such disorders impact each individual differently, the food industry can explore trends and discoveries in encapsulation to produce agonist and antagonist agents to trigger or block specific sensations. Understanding dysosmia and dysgeusia, as well as providing personalized recommendations, will be one of the challenges for the future of nutrition.

6. Conclusion

Healthcare professionals, food science and technology, tasting and somatosensory areas play an important role in creating opportunities and designing specific foods to regain the pleasure of eating not only in individuals infected with COVID-19 but also in other patients suffering from smell and taste disorders (*e.g.*, Alzheimer's and Parkinson diseases, traumatic brain injury, brain tumors, Kallma syndrome and Huntington disease, multiple sclerosis, among others) (Antonini, Leta, Teo, & Chaudhuri, 2020; Høier et al., 2021; Sankrityayan, Kulkarni, & Gaikwad, 2019). Although eating may seem simple, a holistic understanding in different areas is required (food science, materials science, physiology, neurology, chemistry, dentistry, mechanical engineering, psychology, among others).

Future research should combine existing and industrially viable approaches. They can be important innovative tools to stimulate sensory pleasure in patients with olfactory and gustatory disorders. It is too early to say that patients will be completely recovered from such disorders after COVID-19. However, opportunities and innovations in the food industry are wide. Besides, this is the beginning of pioneering multidisciplinary discussions aimed at developing solutions to help individuals regain the pleasure of eating.

Credits authorship contribution statement

Williara Queiroz de Oliveira: Conceptualization, writing - review and editing. **Paulo Henrique Machado de Sousa:** Review and editing. **Glaucia Maria Pastore:** Supervision and funding acquisition.

Ethical approval

This letter does not contain any studies with human participants or animals performed by any of the authors.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

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